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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,097	04/13/2004	Cynthia C. Bamdad	M1015.70013US01	3158

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JHK Law
P.O. Box 1078
La Canada, CA 91012-1078

EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

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03/31/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,097	BAMDAD ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *485, 487-502, 504-507* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

This application, 10823097, with PG Pub No. 20050112607 , filed 04/13/2004 and having 1 RCE-type filing therein and has an effective filing date of 01/25/2000.

Claimed Invention

485. (Currently amended) A method for specifically immobilizing metallic colloid particles comprising: allowing a first metallic colloid particle to become immobilized with respect to a second metallic colloid particle by binding interaction between a first chemical or biological species fastened to the first colloid particle and a second chemical or biological species fastened to the second colloid particle; and determining the immobilization of the first colloid particle with respect to the second colloid particle, wherein at least one of the first or second colloid particle is coated with a self-assembled monolayer (SAM), wherein at least one of the first chemical or biological species or second chemical or biological species is fastened to the first or second colloid particle, respectively, via at least one of a carboxylate group, EDC/NHS chemistry, a nucleic acid sequence, or affinity tag interaction.

Amendment Entry & Claims Status

The amendment filed on January 19, 2010 has been acknowledged and entered.

Claims 485, 487-502, 504 and newly added 505-507 are pending and being examined.

Withdrawn Rejection(s)

Rejection under 112, 2nd paragraph in the previous office action is withdrawn herein.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 485, 487-502, 503-505, 507 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 485 recites “metallic colloid particle" and "colloid particle" which are confusing because it is unclear if these are the same.

Claim 507 recites a "method for detecting specific interaction" in the preamble but fails to recite an active method step of "detecting such specific interaction” in the body of the claim.

Maintained Rejection(s)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 485, 489-502, 504, 505-507 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US 6,984,491) in view of Sigal (US 6,319,670).

Mirkin teaches a method of immobilizing colloid particles comprising allowing a first nanoparticle (colloid) conjugated to first oligonucleotides and a second nanoparticle (colloid) conjugated to second oligonucleotides to bind to each other via the binding of first and second oligonucleotides (see col. 4, line 65-col. 5, line 18). ***Mirkin also teaches that the gold particles can be functionalized with carboxylic acids (carboxylate group) (see col. 38 line 64).*** With respect to claim 489, the oligonucleotides interaction is a biological interaction. With respect to claim 492, oligonucleotides are synthetic molecules. (example 17). With respect to claim 493, the nanoparticles are gold colloid particles. (see col. 71, line 34). With respect to claims 494, 495, 505 and 506, Mirkin teaches that the oligonucleotides on either nanoparticles are labeled with an energy acceptor or donor which are fluorescent molecules (equivalent to emissive or absorptive species and signaling entity of the claimed invention). (see col. 7, line 30). With respect to claims 496, 498, 500, and 504, Mirkin teaches that the first oligonucleotides have a sequence complement to a first portion of the sequence of a target nucleic acid, and the second oligonucleotides have a sequence complement to a second portion of the sequence of the target nucleic acid. The nucleic acid is contacted with the two types of nanoparticles having first and second oligonucleotides under conditions for hybridization of the oligonucleotides with the nucleic acid. (common entity-biological material) (see col. 4, line 65-col. 5, line 18). Regarding claim 507, since Mirkin teaches binding the two first and second

oligonucleotides attached to the first and second gold particles together and attaching a signaling entity to one of those gold particles, a detection of the interaction between the first and second oligonucleotides is also performed. The nucleic acid forms an aggregate of the two nanoparticles. Thus, it is an aggregate forming species. With respect to claim 497, Mirkin teaches the two binding species bind to a common entity which is a colloid particle in figure 13B, the aggregate of nanoparticles. With respect to claims 499 and 501, Mirkin teaches the analyte is a drug (see col. 27, lines 10-12). With respect to claim 502, Mirkin teaches that the analyte can be an enzyme. (see col. 27, lines 40-42).

However, Mirkin fails to teach a self-assembled monolayer and that the first and second species are protein and that the binding interaction is between a protein and a nucleic acid.

Sigal et al. teaches on col. 7, lines 62-68 that assay ligands can be adsorbed onto surfaces by modification of the ligands with moieties that are known to strongly adsorb on the surface, for example thiols will facilitate adsorption of gold. Alternatively, the assay-ligand may be immobilized by adsorption and/or covalent attachment to a "binding layer" coated on the surface of the particle. For example, an assay-ligand may be covalently attached to an oxide surface (e.g., silica or tin oxide) by attachment to functional groups introduced on the surface of the particle (these functional groups may be introduced by methods well-known in the art, e.g., by coating the particle with a self-assembled layer of a functionalized monomer such as a silane. Similarly, an assay-ligand may be covalently attached to the gold surface of a gold particle by coating the

particle by reaction with a functionalized thiol (e.g., to form a self-assembled monolayer). (see col. 8, lines 8-20).

Since it is well known in the art, as taught by Sigal, that a self-assembled monolayer such as thiols layer on gold particles is a layer of moieties that are known to strongly adsorb ligands to the surface of the gold particles, it would have been obvious to one of ordinary skills in the art to coat the gold particles of Mirkin with a SAM as taught by Sigal. Self- assembled monolayer is also known as an orderly layer which, when bound with ligands, provides discrete binding sites on the particles for the target analytes.

Regarding claims 490 and 491, Mirkin has been discussed above for teaching the present invention except that Mirkin discusses on col. 1, lines 55-60, that methods have been reported for making nanoparticles (Quantum dots) water soluble, allowing the immobilization of protein structure on the quantum dot surface. One involves encapsulation of the core-shell structures with a silica layer.

Thus, it would have been obvious to one of ordinary skills in the art to immobilize protein on the nanoparticles and allow the proteins to bind to each other to form aggregate or to bind to a common entity such as a nucleic acid to study protein-protein interaction of a sample in order to diagnose a disease or condition.

Claims 487 and 488 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin in view of Sigal as applied to claim 485 , and further in view of Went (US 6,150,179).

Mirkin and Sigal have been discussed above.

However, Mirkin and Sigal fail to teach that the species fastened to the colloid particle via a metal binding tag.

Went teaches incorporate metal affinity binding tag such as His-tag into proteins so that the proteins can bind to solid phase. (see col. 20, lines 39-40; col. 58, line 49).

It would have been obvious to one of ordinary skills in the art to use the metal binding tag taught by Went as an affinity binding tag to bind the oligonucleotides or proteins to the nanoparticles because the nanoparticles are metals and thus such tag would bind with high affinity to the nanoparticles since it is a metal binding tag.

Response to Arguments

Applicant's arguments filed January 19, 2010 have been fully considered but they are not persuasive.

With regards to the 103 rejection by Mirkin in view of Sigal, Applicants argue the references separately as follows:

With regards to Mirkin, Applicants argue that Mirkin fails to disclose or suggest using self-assembled monolayers (SAM) on the surface of the nanoparticles. Mirkin teaches away from using SAM on its nanoparticle surface. Mirkin fails to teach determining the immobilization of the first colloid particle with respect to the second colloid particle because Mirkin construct cannot be used for detecting single interactions between the colloild particles between a first chemical/biological species fastened to the first and second colloid particles as claimed.

This is not found persuasive because:

while Mirkin fails to teach a SAM, Mirkin teaches determining the interaction between the biological species/oligonucleotides on the nanoparticles because Mirkin teaches using a label/signaling entity to detect the binding of the two species/oligonucleotides. Mirkin fails to teach a SAM. Therefore, a secondary reference, Sigal is applied to teach SAM.

With respect to Applicant's discussion on page 8 of the response regarding claims 486 and 487 where Applicant argues that the office has mischaracterized Mirkin's teaching of the use of biotin-streptavidin being equivalent to the affinity tag interaction used in the present invention, Mirkin's teaching about biotin-streptavidin is no longer being used to equate the affinity tag interaction in the present invention anymore. Claim 486 was cancelled in the previous response filed January 16, 2009 and claim 487 is rejected under 103 by Mirkin in view of Sigal and further in view of Went in the previous office action. Applicant revisitation about this issue is unnecessary. Therefore, no further discussion is necessary.

With respect to Sigal, Applicants argue that Sigal discloses a “binding layer” and col. 8, lines 25-31 in Sigal discloses that the binding layer should be conductive so should not completely coat the surface and should have defect sites. Applicants conclude that Sigal's binding layer is not the same as SAM used in the presently

claimed method. The present application defines SAM as completely covering the surface.

This is not found persuasive because:

Sigal specifically teaches that “assay-ligand maybe covalently attached to the gold surface of the gold particle by coating the particle by reaction with functionalized thiol (e.g. to form a self-assembled monolayer" (see Sigal, col. 8, lines 16-20). Col. 8, lines 24-31 in Sigal discusses that when particles are used as an electrode for generating ECL, a binding layer must have specific characteristics such as being partially coated on the particle as mentioned by Applicants. Otherwise, one of ordinary skills in the art can use the thiol SAM as described in col. 8, lines 16-20.

Applicants further argue that Mirkin and Sigal are not combinable with each other to arrive at the claimed invention because: a person skilled in the art would not be able to modify the nanoparticles with thiol in order to bind proteins and for thiol modified nanoparticles surface, only DNA can be bound thereto.

This is not found persuasive because:

the claimed invention requires “at least one of the first or second colloid particles is coated with a SAM” and claim 490 requires that the interaction comprises binding between a protein and a nucleic acid which means that a protein is fastened to one particle while a nucleic acid is fastened to the other particle. The claims fail to require that the colloid particle that has a SAM is bound to a protein and the claims fail to require that both particles are coated with a SAM. Therefore, by reviewing the teaching

of Sigal, one of ordinary skills in the art can decide that the thiol SAM modified nanoparticle is bound to a DNA while the other particle without a SAM is bound to a protein. Thus, one of ordinary skills can indeed combine the two references.

Applicants further submit that Mirkin only makes aggregates and a fair reading of the Mirkin teaching cannot lead a person of ordinary skill into creating a colloidal structure that can be used to specifically defect another species. Given this disposition, Applicants conclude that Mirkin fails to disclose coating its colloidal with SAM, which would have allowed for a greater level of detection of specific interaction between biological species. Sigal fails to remedy this deficiency because Sigal fails to disclose coating any particle with SAM.

This is not found persuasive because:

Mirkin's structure is used to detect another species as discussed above. Mirkin does not teach a SAM and Sigal, as discussed above, teaches a SAM and both references are combinable as discussed above.

Applicants further submit on page 11 of the response that because Mirkin is narrowly directed to making aggregates, applying SAM to the Mirkin colloidal construct does not promote the aggregation of particles. Rather, naked colloids are significantly more prone to forming aggregates. Therefore, Mirkin discloses a preference for using naked colloids and teaches away from using SAM.

This is not found persuasive because:

Mirkin as discussed in the rejection and the arguments sections, teaches nanoparticles which are coated with oligonucleotides, not naked colloids. The gold particles of Mirkin are also coated with carboxylic acids in order to provide linkers to the oligonucleotides. Therefore the gold particles of Mirkin are not naked colloids and therefore does not teach away from using SAM.

With respect to the 103 rejection for claims 487, 488 by Mirkin in view of Sigal and further in view of Went, Applicants submit the same arguments for Mirkin and Sigal as discussed above and clarifies Went teaching that the metal affinity tag such as His(6) cannot bind to DNA.

Went teaches using a metal affinity binding tag such as His-tag which is bound to a solid phase and His(6) which is attached to a protein to purify proteins using solid phase bound with His-tag.

Again, whether colloidal particles are solid phase and the his-tag can be attached to the colloidal particles as taught by Went while His(6) can bind to a protein.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/
Examiner, Art Unit 1641

/Jacob Cheu/
Primary Examiner, Art Unit 1641